

C.V.

NAME Keith Alan Foster		POSITION TITLE General Project Manager, Research	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Pembroke College, Cambridge University, UK	M.A.	1977	Natural Sciences, majoring in Biochemistry
St Georges Hospital Medical School, University of London, UK	PhD	1980	Biochemistry

A. Positions and Honors.**Positions and Employment**

1980 - 1982	Post Doctoral Fellow, Department of Biochemistry, Queen's Medical School, University of Nottingham, Nottingham, UK.
1982 - 1993	Principal Scientist, SmithKline Beecham Pharmaceuticals Research Division, Epsom, Surrey, UK.
1993 - 1995	Research Group Leader, The Speywood Laboratory Ltd., London, UK
1995 - 1997	Botulinum Fragments Project Manager & Toxin Biology Unit Head, The Centre for Applied Microbiology & Research (CAMR), Porton Down, Salisbury, Wilts. SP4 0JG, UK.
1997 - present	General Project Manager, CAMR, Porton Down, Salisbury, Wilts. SP4 0JG, UK

Other Experience and Professional Memberships

1993 - 1995	Honorary Senior Lecturer: Department of Biochemistry, St George's Hospital Medical School, London, UK
1982	Part-time Tutor with the Open University.
1980 - Present	Member of the Biochemical Society
1985 - Present	Member of Society for Medicines Research
1986 - Present	Member of British Inflammation Research Association
1996 - Present	Member of the Organising Committee for the International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins

B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 26 peer-reviewed publications)

- 1 R.S. Boyd, M.J. Duggan, C.C. Shone & K.A. Foster. The effect of botulinum neurotoxins on the release of insulin from the insulinoma cell lines HIT-15 and RINm5F. *J. Biol. Chem.* 270, 18216-18218 (1995).
- 2 P. Foran, G.W. Lawrence, C.C. Shone, K.A. Foster & J.O. Dolly. BoNT/C1 cleaves both syntaxin and SNAP-25 in intact and permeabilised chromaffin cells: correlation with its blockade of catecholamine release. *Biochemistry* 35, 2630-2636 (1996).
- 3 F. Chen, P. Foran, C.C. Shone, K.A. Foster, J. Melling & J.O. Dolly. Botulinum neurotoxin B inhibits insulin-stimulated glucose uptake into 3T3-L1 adipocytes and cleaves cellubrevin unlike type A toxin which failed to proteolyze the SNAP-23 present. *Biochemistry* 36, 5719-5728 (1997).
- 4 M. Wictome, K.A. Newton, K. Jameson, P. Dunnigan, E. Mackay, S. Clarke, R. Taylor, J. Gaze, K.A. Foster & C.C. Shone. Development of an in vitro bioassay for *Clostridium botulinum* type B neurotoxin in foods that is more sensitive than the mouse bioassay. *Appl. Environ. Microbiol.* 65, 3787-3792 (1999).
- 5 M. Wictome, K.A. Newton, K. Jameson, P. Dunnigan, S. Clarke, J. Gaze, A. Tauk, K.A. Foster & C.C. Shone. The development of novel assays for the detection of botulinum toxins. *FEMS: Imm. Med. Microbiol.* 24, 319-323 (1999).
- 6 M. Welch, J.R. Purkiss & K.A. Foster. Sensitivity of embryonic rat dorsal root ganglia neurons to *Clostridium botulinum* neurotoxin. *Toxicon* 38, 245-258 (2000).
- 7 J. Purkiss, M. Welch, S. Doward & K. Foster. Capsaicin stimulates release of substance P from cultured dorsal root ganglion neurons via two distinct mechanisms. *Biochem. Pharmacol.* 59, 1403-1406 (2000).
- 8 J. Chaddock, J.R. Purkiss, L. Friis, J. Broadbridge, M.J. Duggan, C.C. Shone, C.P. Quinn & K.A. Foster. Inhibition of neurotransmitter release by a retargetted endopeptidase derivative of *C. botulinum* neurotoxin A. *Infection & Immunity*, 68, 2587-2593 (2000).
- 9 J.A. Chaddock, J.R. Purkiss, M.J. Duggan, C.P. Quinn, C.C. Shone & K.A. Foster. A conjugate composed of nerve growth factor coupled to a non-toxic derivative of *Clostridium botulinum* neurotoxin type A can inhibit neurotransmitter release *in vitro*. *Growth Factors*, 18, 147-155 (2000).
- 10 J.A. Chaddock, M.H. Herbert, R. Ling, F.C.G. Alexander, S.J. Fooks, D. Revell, C.P. Quinn, C.C. Shone & K.A. Foster. Expression and purification of catalytically active, non-toxic derivatives of *Clostridium botulinum* toxin type A. *Prot Express Purif.*, 25, 219-228 (2002).

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Chaddock, John Andrew		Senior Scientist	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Durham, UK	BSc.	1988	Molecular Biology / Biochemistry
University of Warwick, UK	Ph.D.	1992	Protein Biochemistry
Open University, UK	Cert. Mgmt	2003	Management

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

Positions and Employment

1992-1995 Postdoctoral Research, University of Warwick, UK
 1995-1996 Postdoctoral Research, University of Warwick, UK
 1996-2001 Scientist, Centre for Applied Microbiology & Research, Salisbury, UK
 2002 – present Senior Scientist, Health Protection Agency, Centre for Applied Microbiology & Research, Salisbury, UK

Other Experience

MSc Examiner in the field of protein toxin biochemistry
 Co-supervisor of Ph.D. studentship at the University of Bath
 Visiting lecturer at University of Bath

Professional Memberships

1988-present Member of Biochemical Society, UK
 2002-present Member of International Association for the Study of Pain

B. Selected peer-reviewed publications (in chronological order).

- Wales, R. Chaddock, J. A., Roberts, L. M. & Lord, J. M. (1992) Addition of an ER retention signal to the ricin A-chain increases the cytotoxicity of the holotoxin. *Exp. Cell Res.*, 203, 1-4.
- Wales, R., Chaddock, J. A., Corben, E. B., Taylor, S. C., Roberts, L. M., Hartley, M. R. & Lord, J. M. (1993) Mutational analysis and possible applications of ribosome-inactivating proteins. In Beadle, D. J., Bishop, D. H. L., Copping, L. G., Dixon, G. K. & Hollomon, D. W. (eds.) BCPC Monograph No. 55: Opportunities for Molecular Biology in Crop Protection, pp99-111.
- Chaddock, J. A. & Roberts, L. M. (1993) Mutagenesis and kinetic analysis of the active site Glu177 of ricin A-chain. *Protein Eng.*, 6, 425-431.
- Chaddock, J. A., Lord, J. M., Hartley, M. R. & Roberts, L. M. (1994) Pokeweed antiviral protein (PAP) mutants which permit *E. coli* growth do not eliminate catalytic activity towards prokaryotic ribosomes. *Nucleic Acids Res.*, 203, 1536-1540.
- Chaddock, J. A., Roberts, L. M., Jungnickel, B. & Lord, J. M. (1995) A hydrophobic region of ricin A-chain which may have a role in membrane translocation can function as an efficient non cleaved signal peptide. *Biochem. Biophys. Res. Commun.*, 217, 68-73.
- Walker, D., Chaddock, A. M., Chaddock, J. A., Roberts, L. M., Lord, J. M. & Robinson, C. (1996) Ricin A-chain fused to a chloroplast-targeting signal is unfolded on the chloroplast surface prior to import across the envelope membrane. *J. Biol. Chem.*, 271, 4082-4085.

7. Chaddock, J. A., Monzingo, A. F., Robertus, J. D., Lord, J. M. & Roberts, L. M. (1996) Major structural differences between pokeweed antiviral protein and ricin A-chain do not account for their differing ribosome specificity. *Eur. J. Biochem.*, 235, 159-166.
8. Hartley, M. R., Chaddock, J. A. & Bonness, M. S. (1996) The structure and function of ribosome-inactivating proteins. *Trends Plant Sci.*, 1, 254-260.
9. Zhan, J., de Sousa, M., Chaddock, J. A., Roberts, L. M. & Lord, J. M. (1997) Restoration of lectin activity to a non-glycosylated ricin B chain mutant by the introduction of a novel N-glycosylation site. *FEBS Lett.*, 407, 271-274.
10. Chaddock, J. A., Purkiss, J. R., Friis, L. M., Broadbridge, J. D., Duggan, M. J., Fooks, S. J., Shone, C. C., Quinn, C. P. & Foster, K. A. (2000) Inhibition of vesicular secretion in both neuronal and nonneuronal cells by a retargeted endopeptidase derivative of *Clostridium botulinum* neurotoxin type A. *Infect. Immun.*, 68, 2587-2593.
11. Chaddock, J. A., Purkiss, J. R., Duggan, M. J., Quinn, C. P., Shone, C. C. & Foster, K. A. (2000) A conjugate composed of nerve growth factor coupled to a non-toxic derivative of *Clostridium botulinum* neurotoxin type A can inhibit neurotransmitter release *in vitro*. *Growth Factors*, 18(2), 147-155.
12. Chaddock, J. A. and Melling, J. (2002) *Clostridium botulinum* and associated neurotoxins. Chapter 55. *Molecular Medical Microbiology*. Ed Max Sussman, Academic Press, London. 1141-1152.
13. Chaddock, JA., Herbert, MH., Ling, R, Alexander, FCG., Fooks, SJ., Revell, D, Quinn, CP., Shone, CC. & Foster, KA. (2002) Expression and purification of catalytically active, non-toxic derivatives of *Clostridium botulinum* toxin type A. *Prot. Express. Purif.*, 25, 219-228
14. Turton, K., Chaddock, JA & Acharya, KR. Botulinum neurotoxins: structure, function and medicine. *TiBS* 2002, 27(11), 552-558.
15. Duggan, MJ, Quinn, CP, Chaddock, JA, Purkiss, JR, Alexander, FCG, Doward, S, Fooks, SJ., Friis, L, Hall, Y, Kirby, ER, Leeds, NJ, Mouldsdale, HJ, Dickenson, A, Green, GM., Rahman, W., Suzuki, Rie, Shone, CC and Foster, KA. Inhibition of release of neurotransmitters from rat dorsal root ganglia by a novel conjugate of a *Clostridium botulinum* toxin A endopeptidase fragment and *Erythrina cristagalli* lectin. *J. Biol. Chem.* 2002, 277(38), 34846-34852.
16. Stancombe, PR, Alexander, FCG, Ling, RJ, Matheson, MA, Shone CC & Chaddock, JA. Isolation of the gene and large-scale expression and purification of recombinant *Erythrina cristagalli* lectin. *Protein Expression & Purification* 2003, 30, 283-292.
17. Chaddock, JA, Duggan, MJ, Quinn, CP, Purkiss, JR, Alexander, FCG, Doward, S, Fooks, SJ., Friis, L, Hall, Y, Kirby, ER, Leeds, NJ, Mouldsdale, HJ, Dickenson, A, Green, GM., Rahman, W., Suzuki, Rie, Shone, CC and Foster, KA. Retargeted clostridial endopeptidases: Inhibition of nociceptive neurotransmitter release *in vitro*, and antinociceptive activity in *in vivo* models of pain. *Movement Disorders* 2004, 19(S8), S42-S47.
18. Hall, YHJ, Chaddock, JA, Mouldsdale, HJ, Kirby, ER, Alexander, FCG, Marks, JD and Foster, KA. Use of a new *in vitro* botulinum neurotoxin antibody detection assay to assess novel vaccine candidates. *J. Immunological. Methods* 2004, 288 (1-2), 55-60
19. Turton, K., Natesh, R., Thiagarajan, N., Chaddock, JA & Acharya, KR. 2004, Crystal structure of *Erythrina cristagalli* lectin with bound N-linked oligosaccharide and lactose. Accepted by *Glycobiology*
20. Sutton, JM, Wayne, J, Scott-Tucker, A, O'Brien, SM, Marks, PMH, Alexander, FCG, Shone, CC and Chaddock, JA. Preparation of specifically activatable endopeptidase derivatives of *Clostridium botulinum* toxins type A, B and C and their applications. Accepted by *Protein Expression & Purification*

In addition, co-inventorship on seven patents:

1. Purkiss, J. R., Chaddock, J. A., Quinn, C. P. & Foster, K. A. Inhibition of secretion from non-neuronal cells. WO 01/21213.
2. Chaddock, J. A., Alexander, F. C. G. & Foster K. A. Preparation of highly pure toxin fragments. WO 01/19863.
3. Foster, K. A., Chaddock, J. A. & Quinn, C. P. Modulation of C-fibre Activity. WO 00/57897A1.
4. Foster, K. A., Chaddock, J. A. & Quinn, C. P. Treatment of mucus hypersecretion. WO 00/10598.
5. Duggan, M. J. & Chaddock, J. A. Conjugates of Galactose-binding Lectins and Clostridial neurotoxins as Analgesics. WO 99/17806.
6. Shone, C. C., Quinn, C. P., Foster, K. A., Chaddock, J. A., Marks, P. R., Sutton, J. M., Stancombe, P. R. & Wayne, J. Recombinant *Clostridium* neurotoxin Fragments. Patent Application No. PCT/GB03/03824.
7. Foster, K.A. & Chaddock, J. A. Retargeted toxin fragments. UK application 0321344.4